

Feasibility of detecting human immunodeficiency virus type 1 drug resistance in DNA extracted from whole blood or dried blood spots

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Abstract:

Due to high cost, availability of human immunodeficiency virus type 1 (HIV-1) drug resistance testing in resource-poor settings is still limited. We therefore evaluated the usefulness of viral DNA extracted from either whole blood or dried blood spots (DBS). Samples were collected from 50 patients receiving therapy and 10 therapy-naive patients. Amplification and sequencing of RNA and DNA was performed using an in-house assay. Protease (PR) and reverse transcriptase (RT) sequences of plasma viral RNA were obtained for 96.6% and 89.7%, respectively, of the 29 patients with a detectable viral load. For cellular viral DNA, useful PR and RT sequences were obtained for 96.6% and 93.1% of the whole-blood-cell samples and for 93.1% and 93.1% of the DBS samples, respectively. For the 31 patients with an undetectable viral load, PR and RT sequences were obtained for 67.7% and 61.3% of the whole-blood-cell DNA preparations and for 54.8% and 58.1% of the DBS DNA preparations, respectively. A good correlation between RNA and DNA sequences was found; most discordances were caused by the detection of mixed amino acids. Of the RT drug-resistant mutations, 13 (38.2%) were seen in RNA only, 6 (17.6%) in DNA only, and 15 (44.1%) in both. Repeated amplification and sequencing of DNA extracts revealed a lack of reproducibility for the detection of drug resistance mutations in a number of samples, indicating a possible founder effect. In conclusion, this study shows the feasibility of genotypic drug resistance testing on whole blood cells or DBS and its possible usefulness for HIV-1 subtyping or examining the overall distribution of drug resistance in a population. For individual patients, RNA sequencing was shown to be superior to DNA sequencing, especially for patients who experienced early treatment failure. The use of DNA extracted from whole blood or DBS for the detection of archived drug resistance mutations deserves further study